EXHIBIT A

Curriculum Vitae

Name: Frank Cuttitta

Date of Birth: November 7, 1947; Brooklyn, New York

Citizenship: United States

Marital Status: Married, 1973, two children

Education:

June 1965	Graduated Wheaton High School Wheaton, Maryland
June 1970	B.A. (Microbiology/Biochemistry), University of Maryland, College Park, Maryland
June 1980	Ph.D. (Microbiology/Immunology), University of Maryland, College Park, Maryland

Brief Chronology of Employment:

1970-1972	Microbiologist GS-5, Platelet Aggregation Studies, Dr. Sherly Johnson, V.A. Hospital, Washington, D.C.
1972-1975	Microbiologist GS-7, Thyroid Research, Dr. Louis Olner, V.A. Hospital, Washington, D.C.
1975-1978	Microbiologist GS-9, Sickle Cell Research, Drs. Geraldine Schechter/Paul McCurdy, V.A. Hospital, Washington, D.C.
1978-1980	Microbiologist GS-11, Monoclonal Antibody Development, Dr. John Minna, V.A. Hospital, Washington, D.C.
1980-1982	NIH Postdoctoral Fellowship, Dr. John Minna, V.A. Hospital, Washington, D.C.
1982-1984	Staff Fellow, NIH, NCI, DCT, Navy Medical Oncology Branch, NNMC, Bethesda, Maryland

1984-1986	Senior Staff Fellow, NIH, NCI, DCT, Navy Medical Oncology Branch, NNMC, Bethesda, Maryland
1986-1989	Research Assistant Professor of Medicine USUHS detailed to NCI-Navy Medical Oncolgy Branch, NNMC, Bethesda, Maryland
1989-1991	Research Associate Professor of Medicine USUHS detailed to NCI-Navy Medical Oncolgy Branch, NNMC, Bethesda, Maryland
1991-1995	Deputy Branch Chief, NIH, NCI, DCS, Biomarkers and Prevention Research Branch, Rockville, Maryland.
1995-1996	Acting Branch Chief, NIH, NCI, DCS, Biomarkers and Prevention Research Branch, Rockville, Maryland.
1997-2006	Senior Investigator, NIH, NCI, CCR, Cell and Cancer Biology Branch, Chief, Cancer Cell Peptide Regulator Section Bethesda, Maryland.
2006-present	Director, NCI Angiogenesis Core Facility Advance Technology Center (ATC) 8717 Grovemont Circle, Room 115 Gaithersburg, MD 20877

Present Address:
7908 Hope Valley Court, Adamstown, Maryland 21710

Telephone:
[redacted]

Mentorship Status-Postdoctoral Teaching Program:

Postdoctoral Fellows

Steve Rosen, M.D. (Northwestern University)	1980-1981
James Mulshine, M.D.	1981-1983

(Holy Cross University)

Sylvia Fargion, M.D. 1981-1983
(Tumor Institute of Milano - Italy)

Austin Doyle, M.D. 1983-1984
(University of Maryland)

Philip Kasprzyk, Ph.D. 1985-1989
(Pennsylvania State University)

Kathryn A. Quinn, Ph.D. 1991-1994
(University of Queensland - Australia)

Theodore Elsasser, Ph.D. 1995-1997
(USDA - sabbatical)

Luis Montuenga, Ph.D. 1995-1998
(University of Navarra - Spain)

Alfredo Martínez, Ph.D. 1994-2004
(University of Navarra - Spain)

Mercedes Garayoa, Ph.D. 1997-1999
(University of Navarra - Spain)

Rubén Pío, Ph.D. 1998-2000
(University of Navarra - Spain)

Enrique Zudaire, Ph.D. 2000-present
(University of Navarra – Spain)

Elizabeth Warner, M.D. 2002-2004
(Department of Surgery, Georgetown University)

Sergio Portal, Ph.D. 2003-present
(University of Navarra – Spain)

Changge Fang, Ph.D. 2007-preesent
(Transfer from NEI)

Mentorship Status - Summer Student Training Program:

Blair High School Magnet Program
Chethan Gangireddy 1995 (summer)

Georgetown Prep High School
Brian Henderson 1996 (summer)

Stone Ridge Country Day School
Christine Piringer 1996 (summer)

Georgetown Prep High School
Brian Henderson 1997 (summer)

Georgetown Prep High School
Brian Henderson 1998(summer)

Georgetown Prep High School
Brian Henderson 1999 (summer)

New York Harbor Health Care Center
Brooklyn, NY
Department of Surgery
Dr. Bridget Chin 2000 (summer)

New York Harbor Health Care Center
Brooklyn, NY
Department of Surgery
Dr. Susan Burekhovich 2002 (summer)

New York Harbor Health Care Center
Brooklyn, NY
Department of Surgery
Ms. Sheba Mathew 2003 (summer)

Alexandria High School
Ms. Christie Falco 2005, 2006 (summer)

Salisbury University
(Eastern Shore Facility)
David Kimmel 2007 (summer)

Bibliographic References

Peer Reviewed Articles

1. Daily, P.O., Cuttitta, F., and MacQuillan, A.M.: The absence of DNA photoreactivation enzyme in yeast mitochondria. **Biochim. Biophys. Acta 454**:375-377, 1976.

2. Cuttitta, F., Rosen, S., Gazdar, A.F., and Minna, J.D.: Monoclonal antibodies that demonstrate specificity for several types of human lung cancer. **Proc. Natl. Acad. Sci. USA 78**:4591-4595, 1981.

3. Minna, J.D., Cuttitta, F., Rosen, S., Bunn, P.A., Carney, D.N., Gazdar, A.F, and Krosnow, S.: Methods for production of monoclonal antibodies with specificity for human lung cancer cells. **In Vitro 17**:1058-1070, 1981.

4. Minna, J.D., Bunn, P.A., Carney, D.N., Cohen, M.H., Cuttitta, F., Fossieck, B.E., Gazdar, A.F., Ihde, D.C., Johnston-Early, A., Matthews, M.J., Oie, H., and Rosen, S.: Experience of the NCI (USA) in the treatment and biology of small cell lung cancer (or: Cancer du poumon a petites cellules: Experience du NCI USA). **Bull Cancer Paris 69**:83-93, 1982.

5. Huang, L.C., Brockhaus, M., Magnani, J.L., Cuttitta, F., Rosen, S., Minna, J.D., and Ginsburg, V.: Many monoclonal antibodies with an apparent specificity for certain lung cancers are directed against a sugar sequence found in acto-N-fucopentose III. **Arch. Biochem. Biophys. 220**:318-320, 1983.

6. Mulshine, J.L., Cuttitta, F., Bribro, M., Fedorko, J., Fargion, S., Little, C., Carney, D.N., Gazdar, A.F., and Minna, J.D.: Monoclonal antibodies that distinguish non-small cell from small cell lung cancer. **J. Immunol. 131**:497-502, 1983.

7. Lindmo, T., Boven, E., Cuttitta, F., Fedorko, J., and Bunn, P.A.: Determination of the immunoreactive fraction of radiolabelled monoclonal antibodies of linear extrapolation to binding at infinite antigen excess. **J. Immunol. Methods 72**:7789-7793, 1984.

8. Rosen, S.T., Mulshine, J.L., Cuttitta, F., Fedorko, J., Carney, D.N., Gazdar, A.F., and Minna, J.D.: Analysis of human small cell lung cancer differentiation antigens using a panel of rat monoclonal antibodies. **Cancer Res. 44**:2052-2061, 1984.

9. Moody, T.W., Carney, D.N., Cuttitta, F., Quattacchi, K., Gazdar, A.F., and Minna, J.D.: Specific binding of bombesin-like peptides to small cell lung cancer cell lines. **Life Sciences 37**:105-113, 1985.

10. Doyle, A., Martin, J., Gazdar, A., Carney, D.N., Nau, M., Cuttitta, F., Mulshine, J., Bunn, P., and Minna, J.D.: Markedly decreased or absent expression of class I histocompatibility antigens in human small cell lung cancer. **J. Exp. Med. 161**:1135-1152, 1985.

11. Cuttitta, F., Carney, D.N., Mulshine, J., Moody, T.W., Fedorko, J., Fischler, A., and Minna, J.D.: Bombesin-like peptides can function as autocrine growth factors in human small cell lung cancer. **Nature (London) 316**:823-826, 1985.

12. Lackie, P., Cuttitta, F., Minna, J.D., Bloom, S., and Polak, J.: Localization of receptors using a dimeric ligand and electron immunocytochemistry. **Histochemistry 83**:57-59, 1985.

13. Gupta, P.K., Myers, J.D., Baylin, S.B., Mulshine, J.L., Cuttitta, F., and Gazdar, A.F.: Improved antigen detection in ethanol-fixed cytological specimens: A modified avidin-biotin-peroxidase complex (ABC) method. **Diagnos. Cytopathol. 1**:133-136, 1985.

14. Cuttitta, F., Carney, D.N., Mulshine, J., Moody, T.W., Fedorko, J., Fischler, A., and Minna, J.D.: Autocrine growth factors in human small cell lung cancer. **Cancer Surveys 4:**707-727, 1985.

15. Sausville, E.A., Lebacq-Verheyden, A.M., Spindel, E.R., Cuttitta, F., Gazdar, A.F., Battey, J.A.: Expression of the gastrin-releasing peptide gene in human small cell lung cancer: Evidence of alternative processing resulting in three distinct mRNAs. **J. Biol. Chem. 261**:2451-2457, 1986.

16. Streicher, H.Z., Cuttitta, F., Buckenmeyer, G.K., Kawamura, H., Minna, J.D. and Berzofsky, J.A.: Mapping the idiotopes of a monoclonal anti-myoglobin antibody with syngeneic monoclonal anti-idiotypic antibodies: Detection of a common idiotype. **J. Immunol. 136**:1007-1014, 1986.

17. Hsu, S.M., Huang, L.C., Hsu, P.L., Ge, Z.H., Ho, Y.S., Cuttitta, F., and Mulshine, J.: Biochemical and ultrastructural study of Leu M1 antigen in Reed-Sternberg cells: Comparison with granulocytes and interdigitating reticulum cells. **J. Natl. Cancer Inst. 77**:363-367, 1986.

18. Fargion, S., Carney, D., Mulshine, J., Rosen, S., Bunn, P., Jewett, P., Cuttitta, F., Gazdar, A., and Minna, J.D.: Heterogeneity of cell surface antigens expression of human small cell lung cancer detected by monoclonal antibodies. **Cancer Res. 46**:2633-2638, 1986.

19. Spitalnik, S.L., Spitalnik, P.F., Dubois, C., Mulshine, J., Magnani, J.L., Cuttitta, F., Civin, C.I., Minna, J.D., and Ginsburg, V.: Glycolipid antigen expression in human lung cancer. **Cancer Res. 46**:4751-4755, 1986.

20. Perez, P., Titus, J.A., Lotze, M.T., Cuttitta, F., Longo, D.L., Groues, E.S., Rabin, H., Durda, P.J., and Segal, D.M.: Specific lysis of human tumor cells by T cells coated with anti-T3 cross-linked to anti-tumor antibody. **J. Immunol. 137**:2069-2072, 1986.

21. Minna, J.D., Battey, J.F., Brooks, B.J., Cuttitta, F., Gazdar, A.F., Johndon, B.E., Ihde, D.C., Lebacq-Verheyden, A.M., Mulshine, J., and Nau, M.M.: Molecular genetic analysis reveals chromosomal deletion, gene amplification, and autocrine

growth factor production in the pathogenesis of human lung cancer. **Cold Spring Harbor Sym Quant. Biol. 51**:843-853, 1986.

22. Carney, D.N., Cuttitta, F., Moody, T.W., and Minna, J.D.: Selective stimulation of small cell lung cancer clonal growth by bombesin and gastrin-releasing peptide. **Cancer Res. 47**:821-825, 1987.

23. Giraud, A.S., Soll, A.H., Cuttitta, F., Walsh, J.H.: Bombesin stimulation of gastrin release from canine gastrin cells in primary culture. **Am. J. Physiol. 252**:G413-G420, 1987.

24. Doyle, L.A., Cuttitta, F., Mulshine, J.L., Bunn, P.A., and Minna, J.D.: Markedly different antibody response to immunized small cell an non-small cell lung cancer cells. **Cancer Res. 47**:5009-5013, 1987.

25. Heikkila, R., Trepel, J.B., Cuttitta, F., Neckers, L.M., and Sausville, E.: Bombesin-related peptides induce calcium mobilization in a subset of human small cell lung cancer cell lines. **J. Biol. Chem. 262**:16456-16460, 1987.

26. Kasprzyk, P.G., Cuttitta, F., Treston, A.M., Avis, I., Nakanishi, Y., Wong, H., Walsh, J.H., and Mulshine, J.L.: Consideration of the chemistry of solid-phase matrix interactions leads to improved quantitation of neuropeptides. **Ann. N. Y. Acad. Sci. 547**:41-53,1988.

27. Lebacq-Verheyden, A.M., Segal, S., Cuttitta, F., and Battey, J.F.: Swiss 3T3 mouse embryo fibroblasts transfected with a human prepro-GRP gene synthesize and secrete Pro-GRP rather than GRP. **J. Cell. Biochem. 36**:237-248, 1988.

28. Reeve, J.R., Cuttitta, F., Vigna, S.R., Shively, J. E., and Walsh, J.H.: Processing of mammalian preprogastrin releasing peptide. **Ann. N. Y. Acad. Sci. 547**:21029, 1988.

29. Cuttitta, F., Fedorko, J., Gu, J., Lebacq-Verheyden, A.M., Linnoila, R.I., and Battey, J.F.: Gastrin releasing peptide gene associated peptides (GGAPs) are expressed in normal human fetal lung and small cell lung cancer: A novel peptide family found in man. **J. Clin. Endocrinol. Metab. 67**:579-583, 1988.

30. Walsh, J.H., Kovacs, T.O.G., Maxwell, V., and Cuttitta, F.: Bombesin-like peptides as regulators of gastric function. **Ann. N. Y. Acad. Sci. 547**:217-224, 1988.

31. Solanki, D.L., McCurdy, P.R., Cuttitta, F., and Schechter, G.P.: Hemolyusis in sickle cell disease as measured by endogenous carbon monoxide production. A preliminary report. **Am. J. Clin. Pathol. 89**:221-225, 1988

32. Nakanishi, Y., Mulshine, J., Kasprzyk, P.G., Natale, R.B., Maneckjee, R., Avis, I., Treston, A.M., Gazdar, A.F., Minna, J.D. and Cuttitta, F.: Insulin-like growth factor-I can mediate autocrine proliferation of human small cell lung cancer cell lines in vitro. **J. Clin. Invest. 82**:354-359, 1988.

33. Mulshine, J.L., Avis, I., Treston, A.M., Mobely, C., Kasprzyk, P.G., Carrasquillo, J.A., Larson, S.M., Nakanishi, Y., Merchant, B., Minna, J.D., and Cuttitta, F.: Clinical use of a monoclonal antibody to bombesin-like peptide in patients with lung cancer. **Ann. N. Y. Acad. Sci. 547**:360-372, 1988.

34. Bhatnagar, M., Springall, D.R., Ghatei, M.A., Burnet, P.W., Hamid, Q., Giad, A., Ibranhim, N.B., Cuttitta, F., Spindel, E.R., Penketh, R., Bloom, S., Polak, J.M.: Localization of mRNA and co-expression and molecular forms of GRP gene products in endocrine cell of fetal human lung. **Histochemistry 90**:299-307, 1988.

35. Nakanishi, Y., Cuttitta, F., Kasprzyk, P.G., Avis, I, Steinberg, S.M., Gazdar, A.F., and Mulshine, J.L.: Growth factor effects on small cell lung cancer cells using a colorimetric assay: Can a transferrin-like factor mediate autocrine growth? **Exp. Cell Biol. 56**:74-85, 1988.

36. Polak, J.M., Hamid, Q., Springall, D.R., Cuttitta, F., Spindel, E., Chatei, M.A., and Bloom, S.R.: Bombesin-like peptides in health and disease. **Ann. N. Y. Acad. Sci. 547**:322-335, 1988.

37. Bepler, G., Zeymer, U., Mahmoud, S., Fiskum, G., Palaszyndki, E., Rotsch, M., Willey, J., Koros, A., Cuttitta, F., and Moody, T.W.: Substance P analogues function as bombesin receptor antagonists and inhibit small cell lung cancer clonal growth. **Peptide 9**:35-45, 1988.

38. Kasprzyk, P.G., Cuttitta, F., Avis, I., Nakanishi, Y., Treston, A., Wong, H., Walsh, J.H., and Mulshine, J.L.: Solid phase peptide quantitation assay using labelled monoclonal antibody and glutaraldehyde fixation. **Anal. Biochem. 174**:224-234, 1988.

39. Carney, D.N., Moody, T., Cuttitta, F.: Bombesin: A potent mitogen for small cell lung cancer. **Ann. N. Y. Acad. Sci. 547**:303-309, 1988.

40. Trepel, J.B., Moyer, J.D., Cuttitta, F., Frucht, H., Coy, D.H., Natale, R.B., Mulshine, J.L., Jensen, R.T., and Sausville, E.A.: A novel bombesin antagonist inhibits autocrine signals in a small cell lung carcinoma cell line. **Biochem. Biophy. Res. Commun. 156**:1383-1389, 1988.

41. Reeve, J.R., Cuttitta, F., Vigna, S.R., Heubrer, V., Lee, T.D., Shively, J.E., Ho, F.J., Fedorko, J., Gazdar, A.F., Minna, J.D., and Walsh, J.H.: Multiple gastrin releasing gene associated peptides are produced by a human small cell lung cancer line. **J. Biol. Chem. 263**:1928-1932, 1989

42. Mulshine, J.M., Avis, I, Treston, A.M., Kasprzyk, P.G., Nakanishi, Y., Mobley, C., Carrasquillo, J.A., Larson, S.M., Merchant, B., Cuttitta, F.: In vvo diagnosis and therapy of human tumors with monoclonal antibodies: Selection of antibodies and preliminary clinical studies in small cell carcinoma of the lung. **Nucl. Med. Biol 16;2**: 159-162, 1989.

43. Mulshine, J.L., Avis, I., Treston, A.M., Kasprzyk, P.G., Nakanishi, Y., Mobley, C., Carrasquillo, J.A., Larson, S.M., Merchant, B., and Cuttitta, F.: In vivo diagnosis and therapy of human tumors and monoclonal antibodies: Selection of antibodies and preliminary clinical studies in small cell carcinoma of the lung. **Int. J. Rad. Appl. Instrum. [B] 16**:159-162, 1989.

44. Mulshine, J.L., Treston, A.M., Natale, R.B., Kasprzyk, P.G., Avis, I., Nakanishi, Y., and Cuttitta, F.: Autocrine growth factors as therapeutic targets in lung cancer. **Chest 96**:31S-34S, 1989.

45. Yang, H., Cuttitta, F., Raybould, H., and Tache, Y.: Intrathecal injection of bombesin inhibits gastric acid secretion in the rat. **Gastroenterology 96**:1403-1409, 1989.

46. Mulshine, J.L., Natale, R.B., Avis, I., Treston, A.M., Kasprzyk, P.G., Nakanishi, Y., and Cuttitta, F.: Autocrine growth factors and lung cancer. **Cancer Treat Res. 45**:107-122, 1989

47. Giacchetti, S., Gauville, C., de Cremoux, P., Bertin, L., Berthon, P., Abita, J.P., Cuttitta, F., and Calvo, F.: Characterization, in some breast cancer cell lines, of gastrin-releasing peptide-like receptors which are absent in normal breast epithelial cells. **Int. J. Cancer 46**:293-298, 1990.

48. Jensen, S.M., Gazdar, A.F., Cuttitta, F., Russell, E.K., and Linnoila, R.I.: A comparison of synaptophysin, chromogranin, and L-dopa decarboxylase as markers for neuroendocrine differentiation in lung cancer cell lines. **Cancer Res. 50**:6068-6074, 1990.

49. Doyle, L.A., Goldstein, L.H., Clingroth, C.J., and Cuttitta, F.: Identification of conditioned medium proteins from human cancer cells adapted to serum-free conditions. **Anal. Biochem. 190**:248-243. 1990.

50. Mahmoud, S., Staley, J., Taylor, J., Bogden, A., Moreau, J.P., Coy, D., Avis, I., Cuttitta, F., Mulshine, J.L., and Moody, T.: [Psi 13,14] bombesin analogues inhibit growth of small cell lung cancer *in vitro and in vivo*. **Cancer Res. 51**:1798-1802, 1991.

51. Mulshine, J.L., Treston, A.M., Scott, F.M., Boland, C., Phelps, R., Kasprzyk, P.G., Nakanishi, Y., Cuttitta, F.: Lung cancer: Rational strategies for early detection and intervention. **Oncology 5**:25- 32, 1991.

52. Avis, I.L., Kovacs,T.O.G., Kaprzyk P.G., Treston, A.M., Bartholomew, R., Walsh, J.H., Cuttitta, F., and Mulshine, J.L.: Preclinical evaluation of an anti-growth factor monoclonal antibody for treatment of patients with lung cancer. **J. Natl. Cancer. Inst. 83**:1470-1476, 1991.

53. Walsh, J.H., Karnes, W.E., Cuttitta, F., and Walker, A.: Autocrine growth factors and solid tumor manignancy. **West J. Med. 155**:152-163, 1991

54. Karnes, W.E., Walsh, J.H., Wu, S.V., Kim, R.S., Martin M.G., Wong, H.C., Mendelson, J., Gazdar, A.F., and Cuttitta, F.: Autocrine stimulation of EGF receptors by TGF-a regulates autonomous proliferation of human colon cancer cells. **Gastroenterology 102**: 474-485, 1992.

55. Mulshine, J.L., Linnoila, R.I., Jensen, S.M., Magnani, J.L., Tockman, M.S., Gupta, P.K., Scott, F.S., Avis, I., Quinn, K., Birrer, J., Treston, A.M., and Cuttitta, F.: Rational targets for the early detection of lung cancer. **J. Natl. Cancer Inst. Monograph 13**: 183-190, 1992.

56. Treston, A.M., Mulshine, J.L. and Cuttitta, F.: Control of tumor cell biology via regulation of peptide hormone processing. **J. Natl. Cancer Inst. Monograph 13**:169-176, 1992.

57. Birrer, M.J., Alani, R., Cuttitta, F., Preis, L.H., Sabichi, A.L., Sanders, D.A., Siegfried, J.M., Szabo, E., and Brown, P.H.: Early events in the neoplastic transformation of respiratory epithelium. **J. Natl. Cancer Inst. Monograph 13**: 31-37, 1992.

58. Mulshine, J.L., Shuke, N., Daghighian, F., Carrasquillo, J., Ghosh, B., Walsh, T., Avis, I., Reynolds, J., Cuttitta, F., Larson, S.M.: The correct dose: Pharmacologically guided end point for anti-growth factor therapy. **Cancer Res. 52 (9 supplement)**: 2743s-2746s, 1992.

59. Quinn, K.A., Treston, A.M., Scott, F.M., Kasprzyk, P.G., Avis, I., Siegfried, J.M., Mulshine, J.L. and Cuttitta, F.: a-Amidation of Peptide Hormones in Lung Cancer. **Cancer Cells 3**: 504-510, 1992.

60. Siegfried, J.M., Kasprzyk, P.G., Treston, A.M., Mulshine, J.L., and Cuttitta, F.: A novel mitogenic peptide amide encoded within the E peptide domain of insulin-like growth factor-IB prohormone. **Proc. Natl. Acad. Sci. 89:**8107-8111, 1992.

61. Scott, F., Cuttitta, F., Treston, A.M., Avis, I., others, Mulshine, A.M.: Prospective trial evaluation immunocytochemical-based sputum techniques for early lung

cancer detection: assays for promotion factors in the bronchial lavage. **J. Cell. Biochem. 17F (supplement):** 175-183, 1993.

62. Martínez, A., Montuenga, L.M., Springall, D.R., Treston, A., Cuttitta, F. and Polak, J.M.: Immunocytochemical localization of peptidylglycine alpha-amidating monooxygenase enzyme (PAM) in human endocrine pancreas. **J. Histochem. Cystochem. 41**: 375-380, 1993.

63. Martínez, A., Burrell, M.A., Kuijk, M., Montuenga, L.M., Treston, A., Cuttitta, F. and Polak, J.M.: Localization of amidating enzymes (PAM) in the rat gastrointestinal tract. **J. Histochem. Cytochem. 41**: 1617-1622, 1993.

64. Mulshine, M.D., Jett, M., Cuttitta, F., Treston, A.M., Quinn, K., Scott, F., Iwai, N., Avis, I., Linnoila, I. and Shaw, G.L.: Scientific basis for cancer prevention. **Cancer 72 (3 supplement)**: 978-983, 1993.

65. Treston, A.M., Scott, F.M., Vos, M., Iwai, N., Mains, R.E., Eipper, B.A., Cuttitta, F. and Mulshine, J.L.: Biochemical characterization of peptide a-amidation enzyme activities of human neuroendocrine lung cancer cell lines. **Cell Growth Diff. 4**: 911-920, 1993.

66. Cuttitta, F.: Peptide amidation: Signature of bioactivity. **Anat. Rec.236**: 87-93, 1993.

67. Moody. T.W. and Cuttitta, F.: Growth factor and peptide receptors in small cell lung cancer. **Life Sci 52**: 1161-1173, 1993.

68. Avis, I., Jett, M., Kasprzyk, P.G., Cuttitta, F., Treston, A.M., Maneckjee, R. and Mulshine. J.L.: Effect of gastrin releasing peptide on the pancreatic tumor cell line (capan). **Mol. Carcino. 8**:214-220, 1993.

69. Mulshine J.L., Cuttitta, F., Scott, F., Quinn, K.A., Shaw, G.L., Avis, I. and Treston, T.: Strategies for lung cancer chemoprevention. **Lung Cancer 9**:357-360, 1993.

70. Clark, D.A., Day, R., Seidah, N., Moody, T.W., Cuttitta, F., and Davis, T.P.: Protease inhibitors suppress in vitro growth of human small cell lung cancer. **Peptides 14**:1021-1028, 1993

71. Steel, J.H., Martinez, A., Springall, D.R., Treston, A.M., Cuttitta, F., and Polak, J.M.: Peptidylglycine a-amidation monooxygenase (PAM) immunoreactivity and messenger RNA in human pituitary and increased expression in pituitary tumours. **Cell Tissue Res. 276**:197-207, 1994.

72. Siegfried, J.M., Han, Y.-H., DeMichele, M.A.,Hunt, J.D., Gaither, A.L. and Cuttitta, F.: Production of gastrin-releasing peptide by a non-small cell lung

carcinoma cell line adapted to serum-free and growth factor-free conditions. **J. Biol. Chem. 269**:8596-8603, 1994.

73. Avis, I., Mathias, A., Unsworth, E.J., Miller, M.J., Cuttitta, F., Mulshine, J.L., Jakowlew, S.B.: Analysis of small cell lung cancer cell growth inhibition by 13-cis-retinoic acid: Importance of bioavailability. **Cell Growth Diff. 6**:485-492, 1995.

74. Martínez, A., Miller, M.J., Quinn, K., Unsworth, E.J., Ebina, M., Cuttitta, F.: Non-radioactive localization of nucleic acids by direct in situ PCR and in situ RT-PCR in paraffin-embedded sections. **J. Histochem. Cytochem. 43**:739-747, 1995

75. Martínez, A., Miller, M.J., Unsworth, E.J., Siegfried J.M., and Cuttitta, F.: Expression of adrenomedullin in normal human lung and in pulmonary tumors. **Endocrinology 136**:4099-4105, 1995.

76. Martínez, A., Unsworth, E.J., and Cuttitta, F.: Adrenomedullin-like immunoreactivity in the nervous system of the starfish *Marthasterias glacialis*. **Cell Tissue Res. 283**:169-172, 1996.

77. Mulshine, J.L., Scott, F., Zhou, J., Avis, I., Vos M., Miller, M.J., Szabo, E., Martínez A., Treston, A.M., Cuttitta, F., and Tockman, M. Development of molecular approaches to early lung cancer detection. **Seminars in Radiation Oncology 6**:72-75, 1996.

78. Quinn, K.A., Treston, A.M., Unsworth, E.J., Miller, M-J., Vos, M., Grimely, C., Battey, J., Mulshine, J.L., and Cuttitta, F. Insulin-like growth factor expression in human cancer cell lines. **J. Biol. Chem. 271**:11477-11483, 1996.

79. Martínez, A., Weaver, C., López, J., Bhathena, S.J., Elsasser, T.H., Miller, M-J., Moody T.W., Unsworth, E.J., and Cuttitta, F. Regulation of insulin secretion and blood glucose metabolism by adrenomedullin. **Endocrinology 137:**2626-2632, 1996.

80. Farah, Z., Jacobs, S., Kull, F., Cuttitta, F., Mulshine, J.L., and Moody, T.M., Monoclonal antibody aIR-3 inhibits non-small cell lung cancer growth in vitro and in vivo. **J. Cell. Biochem. Supplement 24**:269-278, 1996.

81. Miller, M-J., Martínez, A., Unsworth, E.J., Thiele, C.J., Moody, T.W., and Cuttitta, F. Adrenomedulliin: Expression in human tumor cell lines and its potential role as an autocrine growth factor. **J. Biol. Chem. 271**:23345-23351, 1996.

82. Macri, C.J., Martínez, A., Moody, T.W., Gray, K.D., Mitchell, A., Miller, M.J., Gallagher, M., and Cuttitta, F. Detection of adrenomedullin, a hypotensive

peptide, in amniotic fluid and fetal membranes. **Am. J. Obstet. Gynecol. 175**:906-911, 1996.

83. Montuenga, L., Martínez, A., Miller, M.-J., Unsworth, E., and Cuttitta, F. Expression of adrenomedullin and its receptor during embryogenesis suggests autocrine or paracrine modes of action. **Endocrinology 138**:440-451, 1997.

84. Martínez, A., Miller, M.J., Catt K.J., and Cuttitta, F. Adrenomedullin receptor expression in human lung and in pulmonary tumors. **J. Histochem. Cytochem. 45**:159-164, 1997.

85. Mulshine, J.L., Zhou, J., Treston, A.M., Szabo, E., Tockman, M.S., and Cuttitta, F. New approaches to the integrated management of early lung cancer. **Hematol./Oncol. Clin. North Am. 11**:235-252, 1997.

86. Martínez, V., Cuttitta, F., and Taché, Y. Central action of adrenomedullin to inhibit gastric emptying in rats. **Endocrinology 138**:3749-3755, 1997.

87. Moody, T.W., Miller, M.J., Martínez, A., Unsworth, E., and Cuttitta, F. Adrenomedullin binds with high affinity, elevates cyclic AMP and stimulates c-fos mRNA in C6 glioma cells. **Peptides 18**:1111-1115, 1997.

88. Martínez, A., Elsasser, T.H., Muro-Cacho, C., Moody, T.W., Miller, M.J., Macri, C.J., and Cuttitta, F. Expression of adrenomedullin and its receptor in normal and malignant skin: A potential pluripotent role in the integument. **Endocrinology 138**:5597-5604, 1997.

89. Jahnke, G.E., Miller, M.J., Martínez, A., Montuenga, L., and Cuttitta, F. Adrenomedullin expression in the mouse mammary gland: Evidence for the mature form in milk **J. Mol. Endocrin. 19**:279-289, 1997

90. Kelley M.J., Linnoila R.I., Avis I.L., Georgiadis M.S., Cuttitta F., Mulshine J.L., and Johnson B.E. Antitumor activity of a monoclonal antibody directed against gastrin-releasing peptide in patients with small cell lung cancer. **Chest 112**:256-261, 1997.

91. González A., Marin O., Sáchez-Camacho C., Peña J.J., Zudaire E., Martínez A., Cuttitta F., and Muñoz M. Localization of adreomedullin-like immunoreactivity in the hypothalamo-hypophsial system of ampibians. **Neurosci. Lett. 242**:13-16., 1998.

92. Kapas S., Martínez A., Cuttitta, F., and Hinson J.P. Local production and action of adrenomedullin in the rat adrenal zona glomerulosa function. **J. Endocrin. 156**:477-484, 1998.

93. Ravi R.K., Scott F.M., Cuttitta F., Weber E., Kalemkerian G.P., Nelkin B.D., and Mabry M. Induction of gastrin releasing peptide by all-trans retinoic acid in small cell cancer cells. **Oncol. Rep. 5**:497-501, 1998.

94. Martínez A., Farr A., Vos M.D., Cuttitta F., and Treston A.M. Peptide-amidating enzymes are expressed in the stelate epithelial cells of the thymic medulla. **J. Histochem. Cytochem. 46**:661-668, 1998

95. Martínez A., Cuttitta F., and Teitelman G. Expression pattern for adrenomedullin during pancreatic development in the rat reveals a common precursor with other endocrine cell types. **Cell Tissue Res. 293**:141-147, 1998.

96. Montuenga L.M., Zhou J., Avis I., Martinez A., Cuttitta F., Treston A.M., Sunday M., and Mulshine J. Dyanamic changes of expression of heterogeneous nuclear ribonucleoprotein A2/B1 correlated with developmental stages of mammalian lung. **Am. J. Resp. Cell Mol. Biol. 19**:1-9, 1998.

97. Sunday M.E., Yoder B.A., Cuttitta F., Haley K.J., and Emanuel R.L. Bombesin-like peptides mediates lung injury in a baboon model of bronchopulmonary dysplasia. **J. Clin. Invest. 102**:584-594, 1998.

98. Montuenga LM, Mariano JM, Prentice MA, Cuttitta F., and Jakowlew SB. Coordinate expression of transforming growth factor B1 and adrenomedullin in rodent embryogenesis. **Endocrinology 139**:3946-3957, 1998

99. Fernandez-Rodgriquez CM, Prada IR, Prieto J, Montuenga LM, Elsasser T, Quiroga J, Moreiras M, Adreade A, and Cuttitta F. Circulating adrenomedullin in cirrhosis:relationship to hyperdynamic circulation. **J. Hepatol. 29**:250-256, 1998.

100. Montuenga LM, Zhou J, Avis I, Vos M, Martínez A, Cuttitta F, Treston AM, Sunday M, and Mulshine JL. Expression of heterogenous nuclear ribonucleoprotein A2/B1 changes with critical stages of mammalian lung development. **Am. Respir. Cell Mol. Biol. 19**:554-562, 1998.

101. Zaks-Zilberman M., Salkowski C.A., Elsasser T, Cuttitta F., and Vogel S.N. Inductin of adrenomedullin mRNA expression by lipopolysaccharide and paclitaxel (Taxol^{TM}) in murine macrophages. **Infection and Immunity 66**:4669-4675, 1998.

102. Mariano J.M., Montuenga L.M., Prentice M.A., Cuttitta F., and Jakowlew S.B. Concurrent and distinct transcription and translation of tranforming growth factor-□ type I and type II receptors in rodent embryogenesis. **International Journal of Development 42**:1125-1136, 1998

103. Cuttitta F, Montuenga LM, Garayoa M, Pío Rubén, Miller JM, Walsh T, Elsasser T, and Martínez A. The role of adrenomedullin as a growth regulatory peptide in the normal and malignant setting. **J. Animal Sci. 77** (Supplement 3):55-69, 1999

104. Jiménez N, Calvo A, Martínez A, Rosell D, Cuttitta F, and Montuenga LM. Expression of adrenomedullin and proadrenomedullin N-terminal peptide in human and rat prostate. **J. Histochem. Cytochem. 47**:1167-1177, 1999.

105. López J, Cuesta N, Cuttitta F, and Martínez A. Adrenomedullin in nonmammalian vertebrate pancreas: An immunocytochemical study. **Gen. Comp. Endocrinol. 115**:309-322, 1999.

106. Elsasser TH, Kahl S, Martínez A, Montuenga LM, Pío R, and Cuttitta F. Adrenomedullin binding protein in the plasma of multiple species. Characterization by radioligand blotting. **Endocrinology 140**:4908-4911, 1999.

107. Elsasser TH, Sartin JL, Martínez A, Kahl S, Montuenga L, Pío R, Fayer R, Miller MJ, and Cuttitta F. Underlying disease stress augments plasma and tissue adrenomedullin responses to endotoxin: Co-localized increases in adrenomedullin and iNOS within pancreatic istets. **Endocrinology 140**:5402-5411,1999.

108. López J, Cuesta A, Martínez A, Montuenga L, and Cuttitta F. Proadrenomedullin N-terminal 20 peptide (PAMP) immunoreactivity in vertebrate juxta glomerular cells identified by both light and electron microscopy. **Gen. Comp. Endocrinol. 116**:192-203, 1999.

109. Chaudhry A, Carroasquillo JA, Avis IL, Shuke N, Reynolds JC, Bartholomew R, Larson SM, Cuttitta F, Johnson BE, and Mulshine JL. Phase I and imaging trial of a monoclonal antibody directed against gastrin-releasing peptide in patients with lung cancer. **Clin. Cancer Res. 5**:3385-3393, 1999.

110. Martínez A, Elsasser TH, Bhathena SJ, Pío R, Buchanan TA, Macri CJ and Cuttitta F. Is adrenomedullin a casual agent of non-insulin dependent diabetes? **Peptides 20**:1471-1478, 1999.

111. Martínez A, Garayoa M, Pío R, Miller MJ, and Cuttitta F. Adrenomedullin: a new peptide with many clinical implications. **Anales 22**:307-315, 1999.

112. Martínez A, Kapas S, Miller MJ, Ward Y, and Cuttitta F. Coexpression of receptors for adrenomedullin, calcitonin gene related peptide, and amylin in pancreatic b cells. **Endocrinology 141**:406-411, 2000.

113. Serrano J., Uttenthal L.O., Martinez A, Fernandex A.P., Martinez de Velasco J., Alonso D., Bentura M.L., Santacana M., Gallardo J.R., Martinez-Murillo R., Cuttitta F., and Rodrigo J. Distribution of adrenomedullin-like immunoreactivity

in the rat central nervous system by light and electron microscopy. **Brain Res. 853**:245-268, 2000.

114. Moody TW, Coy D, Cuttitta F, Montuenga LM. Proadrenomedullin NH(2)-terminal 20 peptide (PAMP) and adrenomedullin bind to teratocarcinoma cells. **Peptide 21**:101-107, 2000.

115. Elkas J, Armstrong A, Pohl J, Cuttitta F, Martínez A, and Gray K. Modulation of endometrial steroid receptors and growth regulatory genes by tamozifen. **Obstet. Gyneol. 95**:697-703, 2000.

116. Montuenga LM, Burrell MA, Garayoa M, Llopiz D, Vos M, Moody T, García D, Martínex A, Villaro AC, Elsasser T, and Cuttitta F. Expression of proadrenomedullin derived peptides in the mammalian pituitary. Co-localization of FSH and PAMP-like peptide in the same secretory granules of the ganadotorpes. **J. Neuroendo 12:**607-617, 2000.

117. Garayoa M, Martínez A, Lee S, Pío R, An WG, Neckers L, Trepel J, Montuenga LM, Ryan H, Johnson R, Gassmann M, and Cuttitta F. Hypoxia-inducible factor-1 (HIF-1) upregulates adrenomedullin expression in human tumors cell lines during oxygen deprivation: A possible promotion mechanism of carcinogenesis. **Mol. Endocrinol**. **14:**848-862, 2000.

118. Pío R, Martínez A, Elsasser TH, and Cuttitta F. Presence of immunoreactive adrenomedullin (AM) in human and bovine milk: Does AM play a role in the development of the neonate's digestive tract. **Peptides 21**:1859-1863, 2000.

119. Pío R, Martínez A, Unsworth E, Kowalak JA, Bengoechea JA, Elsasser TH, and Cuttitta F. Complement factor H is a serum binding protein for adrenomedullin. The resulting complex modulates the bioactivities of both partners. **J. Biol. Chem. 276**:12292-12300, 2001.

120. Martínez A and Cuttitta F. Adrenomedullin, pancreatic islets, and diabetes. **Canadian J. Diabetes Care 24:**39-46, 2000.

121. Martínez A, Hodge DL, Garayoa M, Young HA and Cuttitta F. Alternative splicing of the proadrenomedullin gene results in differential expression of gene products. **J. Mol. Endocrinology 27**:31-41, 2001.

122. Martínez A, Pío R, López J and Cuttitta F. Expression of the adrenomedullin binding protein, complement factor H, in the pancreas, and its physiological impact on insulin secretion. **J. Endocrinology 170**:503-511, 2001.

123. Pío R, Martínez A, and Cuttitta F. Cancer and diabetes: two pathological conditions in which adrenomedullin may be involved. **Peptides 22**:1719-1729, 2001.

124. Jimenez N, Jongsma J, Calvo A, van der Kwast TH, Treston AM, Cuttitta F, Schroder FH, Montuenga LM, van Steenbrugge GJ. Peptidylglycine alpha-amidating monooxygenase and proadrenomedullin-derived peptide-associated neuroendocrine differentiation are induced by androgen deprivation in the neoplastic prostate. **Int. J. Cancer 94**:28-34, 2001.

125. Chu DQ, Legon S, Smith DM, Costa SK, Cuttitta F and Brain SD. The calcitonin gene-related peptide (CGRP) antagonist CGRP(8-37) blocks vasodilatation in inflamed rat skin: involvement of adrenomedullin in addtion to CGRP. **Neurosci. Lett. 310**:169-172, 2001.

126. Mulshine JL, Hong S, Martínez A, Tauler J, Avis I, Tockman MS, De Luca LM, Placke ME, and Cuttitta F. Moving to the routine management of pre symptomatic lung cancer. **Lung Cancer 34**:Supp2:S1-S5, 2001.

127. Zudaire E, Cuttitta F, and Martínez A. Adrenomedullin, pancreatic physiology and diabetes. **Recent Res. Devel. Endocrinol. 2**:37-54, 2001.

128. Pío R, Elsasser TH, Martínez A, and Cuttitta F. Identification, characterization, and physiological actions of factor H as an adrenomedullin binding protein present in human plasma. **Microsc. Res. Tech. 57**:23-27, 2002.

129. Garayoa M, Bodegas E, Cuttitta F, and Montuenga L. Adrenomedullin in mammalian embryogenesis. **Microsc. Res. Tech. 57**:28-39, 2002.

130. Serrano J, Alonso D, Fernández AP, Encinas JM, López JC, Castro-Blanco S, Ferández-Vizarra P, Richart A, Santacana M, Uttenthal LO, Bentura ML, Martínez-Murillo R, Martínez A, Cuttitta F, and Rodrigo J. Adrenomedullin in the central nervous system. **Microsc. Res. Tech. 57**:76-97, 2002.

131. Cuttitta F, Pío R, Garayoa M, Zudaire E, Julían M, Elsasser TH, Montuenga LM, and Martínez A. Adrenomedullin functions as an important tumor survival factor in human carcinogenesis. **Microsc. Res. Tech. 57**:110-119, 2002.

132. Mulshine JL, Cuttitta F, Tockman MS, and DeLuca LM. Lung cancer evolution to preinvasive management. **Clin. Chest Med. 23**:37-48, 2002.

133. Serrano J, Alonso D, Encinas JM, López JC, Fernández AP, Castro-Blanco S, Richart A, Bentura ML, Santacana M, Uttenthal LO, Cuttitta F, Rodrigo J, Martínez A. Adrenomedullin expression is upregulated by ischemia-reperfusion in the cerebral cortex of the adult rat. **Neuroscience 109**:717-731, 2002.

134. Welsch U, Unterberger P, Höfter E, Cuttitta F, Martínez A. Adrenomedullin in various mammalian and human skin glands including the mammary gland. **Acta Histoclinica 104**:65-72, 2002

135. Isaacs JS, Jung YJ, Mimmaugh EG, Martinez A, Cuttitta F, and Neckers LM. Hsp90 regulates a VHL-independent HIF-1-degradative pathway. **J Biol Chem 277**:24225-24231, 2002.

136. Kane S, Prentice MA, Mariano JM, Cuttitta F, and Jakowlew SB. Differential induction of early response genes by adrenomedullin and transforming growth factor-beta1 in human lung cancer cells. **Anticancer Res 22**:1433-1444, 2002.

137. Martínez A, Vos M, Guédez L, Kaur G, Chen Z, Garayoa M, Pío R, Moody T, Stetler-Stevenson WG, Kleinman HK, and Cuttitta F. The effect of adrenomedullin overexpression in breast tumor cells. **J Natl Cancer Inst 94**:1226-1237, 2002.

138. Seghatoleslami MR, Martínez A, Cuttitta F, and Kosher RA. Distribution and possible function of an adrenomedullin-like peptide in the developing chick limb bud. **Int J Dev Biol 46:**957-961, 2002.

139. Martínez A, Saldise L, Ramírez MJ, Belzunegui S, Zudaire E, Luquin MR, and Cuttitta F. Adrenomedullin expression and function in the rat carotid body. **J Endocrinol 176(1):**95-102, 2003.

140. Garayoa M, Man GO, Martínez A, Cuttitta F, and Mulshine JL. Down-regulation of hnRNP A2/B1 expression in tumor cells under prolonged hypoxia. **Amer J Resp Cell Mol Biol 28:**80-85, 2003.

141. Serrano J, Encinas JM, Fernández AP, Castro-Blanco S, Alonso D, Fernández-Vizarra P, Richart A, Bentura ML, Santacana M, Cuttitta F, Martínez A, and Rodrigo J. Distribution of immunoreactivity for the adrenomedullin binding protein, complement factor H, in rat brain. **Neuroscience 116(4):**947-962, 2003.

142. Martinez A, Pio R, Zipfel PF, Cuttitta F. Mapping of the adrenomedullin binding domains in human complement factor H. **Hypertension Research 26 Suppl:**S55-S59, 2003.

143. Abasolo I, Yang L, Haleem R, Xiao W, Pio R, Cuttitta F, Montuenga LM, Kozlowski JM, Calvo A, and Wang Z. Overexpression of adrenomedullin gene markedly inhibits proliferation of PC3 prostate cancer cell in vitro and in vivo. **Mol Cell Endocrinol 199(1-2):**179-187, 2003.

144. Zudaire E, Cuttitta F, and Martínez A. Regulation of pancreatic physiology by adrenomedullin and its binding protein. **Reg Peptides 112(1-3):**121-130, 2003.

145. Zudaire E, Martínez A, and Cuttitta F. Adrenomedullin and cancer. **Reg Peptides 112(1-3):**175-183, 2003.

146. Macpherson GR, Ng SSW, Forbes SL, Melillo G, Karpova Y, McNally J, Conrads TP, Veenstra TD, Martinez A, Cuttitta F, Price DK and Figg WD. Anti-angiogenic activity of human endostatin is HIF-1- independent *in vitro* and sensitive to timing of treatment in a human saphenous vein assay. **Mol Cancer Therap** 2:845-854, 2003.

147. Martínez A, Julián M, Bregonzio C, Notari L, Moody TW, and Cuttitta F. Identification of vasoactive non-peptidic positive and negative modulators of adrenomedullin using a neutralizing antibody-based screening strategy. **Endocrinology**, 145:3858-3865, 2004.

148. Ajona D, Castaño Z, Garayoa M, Zudaire E, Martínez A, Cuttitta F, Montuenga LM, and Pío R. Complement factor H is expressed by lung cancer cells and protects them from activation of the alternative pathway of complement. **Cancer Res 64:**6310-6318, 2004.

149. Zudaire E, Martínez A, Ozbun LL, and Cuttitta F. Characterization of adrenomedullin in non-human primates. **Biochem Biophys Res Commun 321**:859-869, 2004.

150. Martínez A, Zudaire E, Portal-Núñez, Guédez L, Stetler-Stevenson WG, and Cuttitta F. Proadrenomedullin N-terminal 20 peptide is a potent angiogenic factor and its inhibition results in reduction of tumor growth. **Cancer Res 64:**6489-6494, 2004.

151. Martínez A, Oh H-R, Unsworth EJ, Bregonzio C, Saavedra JM, Stetler-Stevenson WG, and Cuttitta F. Matrix metalloproteinase-2 cleavage of adrenomedullin produces a vasoconstrictor out of a vasodilator. **Biochem J 383**:413-418, 2004.

152. Martínez A, Zudaire E, Julián M, Moody WT, and Cuttitta F. Gastrin-releasing peptide (GRP) induces angiogenesis and the specific GRP blocker 77427 inhibits tumor growth in vitro and in vivo. **Oncogene 24**:4106-4113, 2005.

153. Cuesta N, Martínez A, Cuttitta F, Zudaire E. Identification of adrenomedullin in avian type II pneumocytes: Increased expression after exposure to air pollutants. **J Histochem Cytochem 53**:763-772, 2005.

154. Zudaire E, Cuesta N, Martínez A, and Cuttitta F. Characterization of adrenomedullin in birds. **Gen Comp Endocrin 143**:10-20, 2005.

155. Julián M, Cacho M, García MA, Martín-Santamaría S, de Pasual-Teresa B, Ramos A, Martínez A, and Cuttitta F. Adrenomedullin: a new target for the design of small molecule modulators with promising pharmacological activities. **Eur J Med Chem 40**:7370850, 2005.

156. Zudaire E, Martínez A, Garayoa M, Pío R, Kaur G, Woolhiser MR, Metcalfe DD, Hood WA, Siraganian RP, Guise TA, Chirqwin JM, and Cuttitta F. Adrenomedullin is a cross-talk molecule that regulates tumor and mast cell function during human carcinogenesis. **Am J Pathol 168**:280-289, 2006.

157. Elsasser TH, Capuco AV, Caperna TJ, Martínez A, Cuttitta F, and Kahl S. Adrenomedullin (AM) and adrenomedullin binding protein (AM-BP) in the bovine mammary gland and milk: Effects of stage of lactation and experimental intramammary E. coli infection. **Domest Anim Endocrinol 34**:138-154, 2006.

158. Martínez A, Bengoechea JA, and Cuttitta F. Molecular evolution of proadrenomedullin N-terminal 20 peptide (PAMP): evidence for gene co-option. **Endocrinology 147**:3457-3461, 2006.

159. Rosen D, Lee JH, Cuttitta F, Rafiqi F, Degan S, and Sunday ME. Acceleration thycmi maturation and autoreactive T cell in bronchopulmonry dysplasia. **Am J Respir Crit Care Med 174**:75-83, 2006.

160. Zudaire E, Porta-Nunez S, and Cuttitta F. The central role of adrenomedullin in host defense. **J Leukoc Biol 80**:37-244, 2006.

161. Cuesta N, Nhu OM, Zudaire E, Polumuri S, Cuttitta F, and Vogel SN. IFN regulation factor-2 regulates macrophage apoptosis through a STAT1/3 and caspase-1-dependent mechanism. **J Immunol 178**:3602-3611, 2007.

162. Subramaniam M, Bausch C, Twomey A, Andreeva S, Yoder BA, Change L, Crapo JD, Pierce RA, Cuttitta F, and Sunday ME. Bombesin-like peptides modualte alveolarization and angiogenesis in bronchopulmonary dysplasia. **Am J Respir Crit Care Med 176**:902-912, 2007.

163. Zudaire E, Cuesta N, Murty V, Woodson K, Adams L, Gonzalez N, Martínez A, Narayan G, Kirsch IR, Franklini W, Hirsch F, Birrer M, and Cuttitta F. The aryl hydrocarbon receptor repressor is a putative tumor suppressor gene in multiple human cancers. **J Clin Invest 118(2)**:640-650, 2008.

164. Sackett DL, Pzbun L, Zudaire E, Wessner L, Chirgwin JM, Cuttitta F, and Martínez A. Intercellular proadrenomedullin-derived pepides decorate the microtubules and contribute to cytoskelton function. **Endocrinology 149(6)**:2888-2898, 2008.

165. Kandalaft L, Zudaire E, Portal-Núñez S, Cuttitta F and Jakowlew SB. Testis-specific protein y-encoded-like 2 (TSPYL2) exhibits an inhibitory role on lung tumorigenesis. **Carcinogenesis 129(6)**:1282-1289, 2008.

166. Fernández AP, Serrano J, Tessarollo L, Cuttitta F, and Martínez A. Lack of adrenomedullin in the mouse brain results in behavioral changes, anxiety, and

lower survival under stress conditions. **Proc Natl Acad Sci USA 105(34)**:12581-12586, 2008.

167. Garatziotis S, Zudaire E, Trempus CS, Hollingsworth JW, Jiang D, Lancaster LH, Richardson E, Zhuo L, Cuttitta F, BrownKK, Noble PW, Kimata K, and Schwartz DA. Serum inter-alpha-trypsin inhibitor and matrix hyaluronan promotes angiogenesis in fibrotic lung injury. **Am J Repir Crit Care Med 178(9)**:939-947, 2008.

168. Kwon M, Hanna E, Lorang D, He M, Quick JS, Adem A, Stevenson C, Chung JY, Hewitt SM, Zudaire E, Esposito D, Cuttitta F, and Libutti S. Functonal characterization of filamin a interacting protein 1-like, a novel candidate for antivascular cancer therapy. **Cancer Res. 68(18)**:7332-7341, 2008.

169. El-Chemaly S, Malide D, Zudaire E, Ikeda Y, Weinberg BA, Pacheco-Rodriguez G, Rosas IO, Aparicio M, Ren P, MacDonald SD, Wu HP, Nathan SD, Cuttitta F, McCoy JP, Gochuico BR, and Moss J. Abnormal lymphangiogenesis in idiopathic pulmonary fibrosis with insights into cellular and molecular mechanisms. **Proc Natl Acad Sci USA 106(10)**:3958-3963, 2009.

170. Fang C, Aparicio M, Avis I, Martínez A, Zudaire E, and Cuttitta F. Non-peptide small molecule regulators of lymphangiogenesis. **Lymphat Res Biol. 7**:189-196, 2009.

Book Chapters

1. Minna J.D., Carney, D.N., Alvarez R., Bunn, P.A., Cuttitta, F., Ihde, D.C., Matthews, M.J., Oie, H., Rosen, S., Whang-Peng, J., and Gazdar, A.F.: Heterogeneity and homogeneity of human small cell lung cancer. In *Tumor Cell Heterogeneity*. Edited by Owens, A.H., Coffey, D.S., & Baylin, S.B., Academic Press, N.Y., pp 29-52, 1982.

2. Minna, J.D., Carney, D.N., Cuttitta, F., and Gazdar, A.F.: The biology of lung cancer. In *Rational Basis for Chemotherapy*. Alan R. Liss Incorporated, N.Y., pp1-22, 1983.

3. Cuttitta, F., Rosen, S., Carney, D.N., Gazdar, A.F., and Minna, J.D.: Monoclonal antibodies against human lung cancer: Potential diagnostic and therapeutic use. In *Biology and Management of Lung Cancer*. Edited by Greco, F.A., Martinue Nijhoff Publishers, N.Y., pp 1-22, 1983.

4. Carney, D.N., Gazdar, A.F., Oie, H.K., Cuttitta, F., and Minna, J.D.: The in vitro growth and characterization of small cell lung cancer. In *Biology and Management*

of Lung Cancer. Edited by Greco, F.A., Martinue Nijhoff Publishers, N.Y., pp 25-41, 1983.

5. Minna, J.D., Carney, D.N., Cuttitta, F., Gazdar, A.F., Ihde, D.C., Mulshine, J.L., and Nau, M.: Clinical, cellular, and molecular biology of lung cancer. In *Adjuvant Therapy of Cancer IV.* Edited by Jones, S.E. & Salmon, S.E., Grune & Stratton Publishers, N.Y., pp 167-182, 1984.

6. Carney, D.N., Gazdar, A.F., Cuttitta, F., and Minna, J.D.: In vitro studies of the biology of lung cancer. In *Lung Cancer: Causes and Prevention.* Edited by Simmon, S.E., Verlag Chemie International, pp 247-261, 1984.

7. Cuttitta, F., Rosen, S., Carney, D.N., Fedorko, J., Gregorio, T., Stephenson, S., Mulshine, J.L., Fargion, S., Abrams, P.G., Moody, T.W., Gazdar, A.F., and Minna, J.D.: Monoclonal antibodies to human lung tumor antigens. In *Monoclonal Antibodies and Cancer.* Edited by Wright, G.L., Marcel Dekker, N.Y., pp161-180, 1984.

8. Cuttitta, F., Carney, D.N., Mulshine, J.L., Fedorko, J., Fargion, S., Fischler, A.: Monoclonal antibodies against endocrine tumors of the human lung. In *The Endocrine Lung in Health and Disease.* Edited by Becker, K.L. & Gazdar, A.F., W.B. Saunders Company, Philadelphia, pp 488-500, 1984.

9. Mulshine, J.L., Cuttitta, F., and Minna, J.D.: Lung Cancer Markers as detected by Monoclonal antibodies. In *Monoclonal Antibodies in Cancer.* Edited by Sell, S. & Reusfeld, R.A., Humana Press, N.Y., pp 229-246, 1985.

10. Browning, M.D., Linnoila, I., Funa, K., Cuttitta, F., Worsham, G.F., Fargion, S., Minna, J.D., and Mulshine, J.L: The role of monoclonal antibodies in lung cancer. In *Monoclonal Antibodies in Cancer: Advances in Diagnosis and Treatment.* Edited by Roth, J.A., Futura Publishing Company, N.Y., pp 87-109, 1986.

11. Mulshine, J.L., Minna, J.D., Cuttitta, F., et al.: Antigens related to lung cancer. In *Tumor Associated Antigens and Other Markers.* Edited by Ghosh, B., McGraw-Hill Publishers, N.Y., pp 121-133, 1986.

12. Minna, J.D., Cuttitta, F., Mulshine, J.L., Bunn, P.A., Carney, D.N., Doyle, A., Fedorko, J., Gazdar, A.F., Linnoila, I., Nau, S., and Rosen, S.: New approaches to using monoclonal antibodies in the diagnosis and treatment of lung cancer. In *Lung Cancer: University of Texas Annual Clinical Conference on Cancer Vol 28.* Edited by Mountain, C.F., & Carr, D.T., pp 345-350, 1987.

13. Minna, J.D., Battey, J.F., Birrer, M., Brooks, B., Cuttittta, F., DeGreve, J., Gazdar, A.F., Johnson, B., Nau, M., Sausville, E., Seifter, E., and Vinocour, M.: Chromosomal deletion, gene amplification, alternative processing and autocrine growth factor production in the pathologenesis of human lung cancer. In

Oncogenes and Cancer. Edited by Aaronson, S.A., Japan Science Society Press, Tokyo, pp109 -122, 1987.

14. Minna, J.D., Cuttitta, F., Battey, J., Mulshine, J., Linnoila, I., Gazdar, A.F., Trepel, J., and Sausville, E.: Gastrin-releasing peptide and other autocrine growth factor in lung cancer: Pathogenetic and treatment implications. In *Important Advances in Oncology*. Edited by DeVita, V., Hellman, S., & Rosenberg, S., J.B. Lippincott Company, Philadelphia, pp 55-64, 1988.

15. Mulshine, J.L., Kasprzyk, P.G., Nakanishi, Y., Avis, I., Seifter, E., and Cuttitta, F.: Considerations in the development of clinical trials employing monoclonal antibodies. Proceedings of the First International Workshop on Small Cell Lung Cancer Antigens. In *Lung Cancer*. Vol. 4, pp 81-83, 1988.

16. Moody, T.W., O'Donohue, T.L., Chronwall, B.M., Cuttitta, F., Linden, C.D., Getz, R.L., and Wolf, S.S.: Neurochemistry and pharmacology of bombesin-like peptides. In *Polypeptide Hormones: Mechanisms of Action*. Edited by Negro/Vilar, A. & Cohen, M., CRC Press, Boca Raton, pp 3-40, 1988.

17. Gazdar, A.F., Oie, H., Cuttitta, F., Nakanishi, Y., Linnoila, I., and Mulshine, J.L.: Peptide production and stimulation of neuroendocrine (NE) cells and tumors of the lung. Beltsville Symposium XII. In *Biomechanisms Regulating Growth and Development*. Edited by Steffens, Rumsey, & Norvell, Martines and Nyhoff Publishers, pp 157-170, 1988.

18. Treston, A.M., Kasprzyk, P.G., Covey, T., Lee, E.D., Henion, J., Yergey, A., Cuttitta, F. and Mulshine, J.L.: Mass Spectrometric Identification and Sequencing of Novel Neuropeptides. In *Annals of the New York Academy of Sciences*, Vol. 547, pp 438-440, 1988.

19. Treston, A.M., Yergey, A., Kasprzyk, P.G., Cuttitta, F., and Mulshine, J.L.: Application of mass spectrometry to the identification of novel peptide hormones involved with lung cancer biology. In *Biology of Lung Cancer*. Edited by Rosen, S.T., Mulshine, J.L., Cuttitta, F., & Abrams, P.G., Marcel Dekker Publishers, N.Y., pp 91-119, 1988.

20. Nakanishi, Y., Cuttitta, F., Kasprzyk, P.G., Treston, A.M., Avis, I., Minna, J.D., Kleinman, H.K., and Mulshine. J.L.: The effects of growth factor on the in vitro growth of small cell lung cancer biology. In *Biology of Lung Cancer*. Edited by Rosen, S.T., Mulshine, J.L., Cuttitta, F., & Abrams, P.G., Marcel Dekker Publishers, N.Y., pp 59-89, 1988.

21. Minna, J.D., Battey, J.F., Birrer, M., Cuttitta, F., DeGreve, J., Gazdar, A.F., Ihde, D., Johnson, B., Kaye, F., Krystal, G., LeBacq, A.M., Linnoila, I., Mulshine, J.L., Nau, M., Sausville, E., Schutte, J., and Trepel, J.: Genetic changes involved in the pathogenesis of human lung cancer including oncogene activation chromosomal

deletions and autocrine growth factor production. In *Accomplishments in Cancer Research.* Edited by Fortner & Rhoads, J.B. Lippincott Company, Philadelphia, pp 155-182, 1988.

22. Cuttitta, F., Kasprzyk, P.G., Treston, A.M., Avis, I., Jensen, S., Levitt, M., Siegfried, J., Mobley, C., and Mulshine, J.L.: Autocrine growth factors that regulate the proliferation of pulmonary malignancies in man. In *Biology, Toxicology and Carcinogenesis of Respiratory Epithelium.* Edited by Thomassen, D.G & Nettesheim, P., Hemisphere Publishing Corporation, N.Y., pp228-270, 1990.

23. Cuttitta, F.: Autocrine/paracrine growth factors and human malignancies. In *Gastrointestinal Endocrinology: Receptors and Post-Receptor Mechanisms.* Edited by Thompson, J.C., Academic Press Incorporated, N.Y., pp455-478, 1990.

24. Siegfried, J.M., Birrer, M., and Cuttitta, F.: Detection of growth factor effects and expression in normal and neoplastic human bronchial epithelial cells. In *Transformation of Human Epithelium: Molecular and Oncogeneic Mechanisms.* Edited by Milo, G.E. & Casto, B.C., CRC Press, Baco Raton, pp13-29, 1992.

25. Cuttitta, F., Treston, A., Siegfried, J., Quinn, K., Avis, I., Scott, F., and Mulshine, J.: Peptide physiology of human cancer cells and its relationship with autocrine/paracrine growth. In *Diagnostic Histopathology of Neuroendocrine Tumors.* Edited by Polak, J.M., Churchill Livingstone, London, pp15-39, 1993.

26. Mulshine, L.J., Szabo, E., Scott, F., Quinn, K., Zhou, J., Avis, I., Miller, M.J., Vos, M., Treston, A.M., Cuttitta, F., and Shaw, G.L.: The sceeening for and early detection of lung cancer. In *Lung Cancer.* Edited by Carney D.N., Aronald, London, pp3-11, 1995.

27. Cuttitta, F., Miller, M.J., Montuenga, L., Garayoa, M., Elsasser, T., Walsh, T., Unsworth, E., and Martínez, A. Adrenomedullin - Terra Incognita. In *Adrenomedullin.* Edited by Martínez A. and Cuttitta F., IOS Press, Amsterdam, pp1-26, 1998.

28. Miller, M.J., Martínez, A., Montuenga, L., Garayoa, M., Moody, T., Unsworth, E., and Cuttitta, F. Adrenomedullin: A pluripotent peptide with growth regulatory function. In *Adrenomedullin.* Edited by Martínez A. and Cuttitta F., IOS Press, Amsterdam, pp 171-184, 1998.

29. Montuenga, L.M., Martínez, A., Miller, M.J., Garayoa, M., Elsasser, T., and Cuttitta, F. Expression of AM and PAMP in normal adult and developing mammals. In *Adrenomedullin.* Edited by Martínez A. and Cuttitta F., IOS Press, Amsterdam, pp 49-68, 1998.

30. Martínez, A., Miller, M.J., Montuenga, L., and Cuttitta, F. Adrenomedullin regulates hormone secretion. In *Adrenomedullin.* Edited by Martínez A. and Cuttitta F., IOS Press, Amsterdam, pp 185-196, 1998.

31. Mulfoz, M., Zudaire, E., Martínez, A., Cuttitta, F., and Gaonzález, A. Adrenomedullin-like immunoreactivity in the central nervous system of the frog, Rann perezi. In *Adrenomedullin.* Edited by Martínez A. and Cuttitta F., IOS Press, Amsterdam, pp 267-288, 1998.

32. Rodrigo, J., Serrano, J., Martínex de Velasco, J., Fernández, A.P., Bentura, M.L., Santacana, K., Uttenthal, L.O., Pedrosa, J.A., Peinado, M.A., Gallardo, J.R., Martínez, A., Martínez-Murillo, R., and Cuttitta, F. Distribution of adrenomedullin-like immunoreactivty in the rat cental nervous system: A light and electron microscopic study. In *Adrenomedullin.* Edited by Martínez A. and Cuttitta F., IOS Press, Amsterdam, pp 289-386, 1998.

Books Edited

1. Steve Rosen, James L. Mulshine, Frank Cuttitta, and Paul Abrams, Editors. Biology of Lung Cancer: Diagnosis and Treatment. New York, Marcel Dekker, 1988.

2. Alfredo Martínez and Frank Cuttitta, Editors. Adrenomedullin. Amsterdam, IOS Press, 1998.

3. Enrique Zudaire and Frank Cuttitta, Editors, Textbook of Angiogenesis and Lymphangiogenesis Assay Methodology and Use. Springer, 2011.

Publications Issued By Department Of the U.S. Government:

Martínez, A. and Cuttitta, F.: Bringing together morphologists and molecular biologists: In situ PCR and RT-PCR. In *The NIH Catalyst.* Edited by Liotta, L.A., Vol. 3, Issue 3, 1995, pp. 12-13, & 22.

International Meeting - Organized/Sponsored

NCI Adrenomedullin Symposium, September 3-5, 1997, Nathcher Building, Main NIH Campus, Bethesda, Maryland.

Patents Held Through U.S. Government Participation:

Monoclonal antibody 2A11 filed for Patent Pending Status
Neutralizing antibody to the tumor growth factor gastrin releasing peptide,
Application supported by the documentation
presented in Cuttitta *et al.* **Nature (London) 316**:823-826, 1985
Filing Date - September 9, 1985
First Revision of Patent - June 20, 1989

Second Revision of Patent - September 10, 1990
Final Patent Awarded - February 13, 1991

US Government International Patents/US Government Provisional Patents:

Monoclonal antibody 2A11 as detection assay for SCLC
Initial Filing Date - March 5, 1991
Second Revision of Patent - February 10, 1994

Monoclonal antibody 2All as therapeutic approach to SCLC
Initial Filing Date - March 5, 1991
Second Revision of Patent - February 10, 1994

Monoclonal antibody G6 filed for Patent Pending Status
Neutralizing antibody to the tumor cell growth factor adrenomedullin, Application supported by the documentation presented in Miller *et al.* **J. Biol. Chem. 271(38)**:23345-23351, 1996
Filing Date - August 30, 1995

Adrenomedullin suppresses insulin release while MoAB-G6 augments insulin secretion - Implicate potential role in diabetes
Application supported by the documentation presented in Martínez *et al.* **Endocrionology 137(6)**:2626-2632, 1996
Filing Date - August 30, 1995

Adrenomedullin involvement in fetal development, implantation and preeclampsia
Application supported by the documentation presented in Macri *et al.* **Am J Obstet Gynecol 175**:906-911, 1996 and Montuenga *et al.* **Endocrinology 138(1)**:440-451, 1997
Filing Date - August 30, 1995

Functional role of adrenomedullin (AM) and the gene related product (PAMP) in human pathology and physiology.
U.S. Patent Application No. 09/011,922
Filing Date – August 16, 1996.

Functional role of adrenomedullin (AM) and the gene related product (PAMP) in human pathology and physiology.
Japan Patent Application No. 509499/97.
Filing Date – August 16, 1996.

Functional role of adrenomedullin (AM) and the gene related product (PAMP) in human pathology and physiology.
United Kingdom Patent Application No. 0 845 036
Filing Date – August 16, 1996.

Identification of a serum binding protein for adrenomedullin and the functional role it has on adrenomedullin mediated biology.
Application supported by the documentation presented in
Elsasser T *et al.* **Enodcrinology 140**:4908-4911, 1999.
Filing Date - September 10, 1999.

Determination of adrenomedullin-binding proteins.
Canada Patent Application No. 2,383,419
Filing Date – September 8, 2000.

Determination of adrenomedullin-binding proteins.
Application supported by the documentation presented in
Pío R *et al.* **J. Biol. Chem. 276**:12292-12300, 2001.
Complement factor H identified as a serum binding protein for adrenomedullin (AM) and when complexed with AM enhances the ligand's biological activity.
US Provisional Patent No. 10/070/853
Filing Date – August 26, 2002

Vassopressor peptide derived from adrenomedullin and methods of its use.
Demonstrates matrix metalloprotease-2 (MMP-2) rapidly degrades AM and destroys the ligand's hypotensive property. MMP-2 enzymatic cleavage of AM is completely blocked when the peptide ligand is complexed with complement factor H. Also, a fragmentary peptide from the AM/MMP-2 degradative process, denoted as AM11-22, functions as a hypertensive peptide.
U.S Provisional Patent Application No. 60/416,291
Filing Date – October 4, 2002.

A new target for angiogenesis and anti-angiogenesis therapy.
Identification of proadrenomedullin N-terminal peptide (PAMP) as a potent tumor-derived angiogenic factor and a peptide antagonist to PAMP which blocks angiogenesis and suppresses xenograft growth.
U.S. Provisional Patent Application No. 60/425,018
Filing Date – November 7, 2002.

Non peptide agonist and antagonist of adrenomedullin and gastrin-releasing peptide.
Development of a new robust methodology for identifying small molecule regulators of peptide hormone function base on the disruption of neutralizing monoclonal antibodies binding to appropriate ligands.
Establishing gastrin-releasing peptide (GRP) as a potent tumor-derived angiogenic factor and identifying a small molecule antagonist that blocks GRP angiogenic activity and suppresses xenograft formation in nude mouse studies.
U.S Provisional Patent Application No. 60/500,650
Filing Date – September 8, 2003

Stably transfected multicolored fluorescent cells.

Generation of human tumor cell lines and endothelial cell lines with different colored fluorescent proteins (GFP, YFP, RFP, & CFP) for use in co-culture angiogenesis assays.
U.S. Provisional Patent Application No.60/976,732
Filing Date – October 1, 2007

Apelin peptides and methods of use.
Identification of a unique amidated peptide process from the N-terminus of apelin-36 that has potent angiogenic activity.
U.S. Provisional Patent Application No. 61/156.351
Filing Date - February 27, 2009

Antiangiogenic small molecules, and methods of use.
Screening of the DTP small molecule diversity set of small molecules has identified several compounds that disrupt endothelial cells growth or tube formation and suppress xenograft human tumor cell growth.
U.S. Provisional Patent Application No. 61/230,667
Filing Date – July 31, 2009

Methods of monitoring angiogenesis and metastasis in three dimensional co-cultures.
Use of human tumor cell xenograft biopsy implants in 3D co-cultures with endothelial cells to determine antiangiogenic drug sensitivity profile – prototype assay as "Proof-of-Principle" for clinical application segue.
U.S. Provisional Patent Application No. 12/802,666
Filing Date – June 10, 2010

Confidential Disclosure Agreements (CDA)/Material Transfer Agreements (MTA)/Cooperative Research and Development Agreements (CRADA) with US Biomedical/Pharmaceutical Companies:

Evogenix CRADA ($300,000) – Initiated November 1, 2006. Pre-clinical evaluation of a humanized neutralizing anti-proadrenomedullin N-terminal 20 peptide (PAMP) monoclonal antibody as an antiangiogenic drug.

Sisene CRADA ($200,000) – Initiated July 10, 2010. Pre-clinical evaluation of recombinant C-terminal Nephroblastoma Over Expressed Protein (NOV)/Cysteine Rich Protein 61, Connective Tissue Growth Factor, Nephroblastoma Over Expressed Protein (CCN3) as an antiangiogenic drug. In addition, determine the mechanism of action underlying the antiangiogenic effect.

Millipore Corporation CDA to discuss neutralizing compounds that block adrenomedullin biological activity and parallel discussion on related peptide amide growth factors. Initiated July 1, 2010.

Salk Institute MTA for neutralizing anti-bombesis/gastrin releasing peptide monoclonal antibody. Initiated July 19, 2010.